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Research Article

ELUCIDATING THE NEUROTOXICOPATHOLOGICAL IMPACT OF MICRO AND NANOPLASTICS: MECHANISTIC INSIGHTS INTO OXIDATIVE STRESS-MEDIATED NEURODEGENERATION AND IMPLICATIONS FOR PUBLIC HEALTH IN A PLASTIC PERVASIVE ERA

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Abstract

This study synthesizes current insights into the neurotoxic effects of micro- and nano-plastics (MNPs) on the central nervous system. Growing evidence links MNP exposure to the development of neurodegenerative diseases. The study focuses on how these plastic particles induce oxidative stress, neuroinflammation, and cellular homeostasis disruption. Key mechanisms include lipid peroxidation, DNA damage, protein misfolding, and neuronal death. It also explores alterations in gene expression related to neurotransmission and antioxidant defense, emphasizing the complex interaction between the physicochemical properties of MNPs and their neurobiological impact. By comparing MNP-induced effects with those of known neurotoxic agents, the research identifies critical gaps in knowledge particularly regarding dose-response relationships, chronic exposure, and the impact of different polymer types and additives. The study concludes by advocating for multidisciplinary research to develop better detection tools, protective strategies, and public health policies to address the emerging neurological threats posed by MNP pollution.

Keywords: Microplastics, Nano Plastics, Neurotoxicity, Oxidative Stress, Neuroinflammation, Blood-Brain Barrier, Neurodegenerative Diseases, Plastic Pollution.

1. Introduction

The worldwide surge in plastic manufacture has precipitated a significant environmental disaster with extensive repercussions for ecosystems and human health. In 2019, over 368 million metric tons of plastic were manufactured globally[1]. By 2050, it is projected that around 12 billion metric tons of microplastics would exist in the environment[2-3]. The escalating issue was exacerbated by the COVID-19 pandemic by the extensive utilization of disposable plastic products, including gloves, masks, and face shields. Countries in Southeast Asia, including Indonesia, Malaysia, and the Philippines, have experienced the most significant increase in microplastic contamination. The escalating issue was exacerbated by the COVID-19 pandemic by the extensive utilization of disposable plastic products, including gloves, masks, and face shields. Individuals in these areas are projected to consume around 15 grams of microplastics monthly. Simultaneously, areas throughout East Asia,

Africa, Europe, and the Americas have witnessed a substantial rise in microplastic concentrations since the 1990s, underscoring the worldwide scope of the epidemic[4]. Microplastics and nano plastics are little plastic particles that pose a growing concern to environmental and public health[5]. Microplastics are described as plastic particles measuring less than 5 millimetres, and nano plastics are generally less than 1 micrometre[6]. In certain definitions, nano plastics are defined as being smaller than 100 nanometres[7-8]. These particles have remarkable environmental persistence, frequently requiring centuries to decompose. Owing to their diminutive dimensions, they can effortlessly infiltrate aquatic environments, soil, food products, and even the atmosphere. The gradual degradation of bigger polymers by sunshine, water, and wind results in the formation of smaller particles, although the process is seldom fully realized. A restricted number of bacteria possess the capability to degrade plastic, rendering the accumulation of these particles nearly inevitable[9]. The predominant varieties of plastic waste encountered in the environment are polyethylene, polypropylene, polystyrene, and polyvinyl chloride[10]. These plastics accumulate in aquatic environments, including rivers, lakes, and oceans, disrupting biodiversity and impacting the health of marine creatures. Human exposure to microplastics and nano plastics transpires through various pathways, including inhalation and ingestion. Individuals can inhale airborne particles in both indoor and outdoor settings; however, indoor situations typically exhibit elevated amounts due to restricted air circulation[11]. Infants and children, who predominantly remain indoors, are particularly susceptible to this type of exposure. Waterborne exposure constitutes another significant route for these particles. Humans can ingest microplastics through tap water, bottled beverages, tea, soft drinks, or beer[12]. Moreover, other food products such as seafood, sugar, honey, and salt have been discovered to contain these little plastic particles[13]. This is particularly alarming for young children, whose developing bodies are more susceptible to the detrimental effects of plastic pollution. As exposure escalates via direct contact and the food chain, the likelihood of enduring health hazards, including inflammation, organ damage, and neurological illnesses, intensifies.

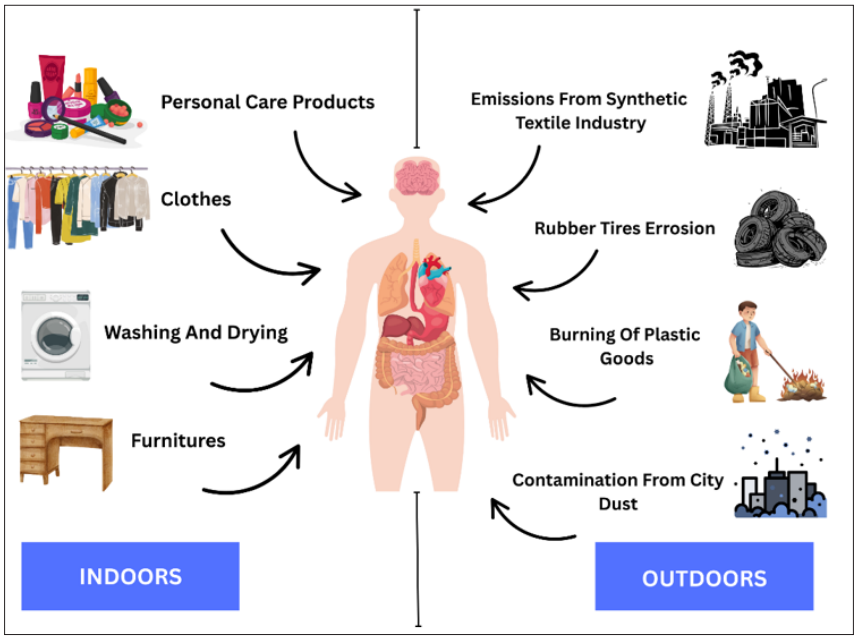

Figure 1: Exposure to micro and nano plastics can occur through several common routes. According to reports from the world health organization and the european food safety authority, humans are regularly exposed to varying amounts of these particles in everyday life, primarily through ingestion and inhalation[14-16]

2. Routes of Microplastic Entry into the Body

Microplastics have demonstrated the ability to penetrate the central nervous system via multiple biologically relevant pathways, presenting considerable risks to neurological health. Inhalation is one of the most significant direct entrance routes[17]. Airborne microplastic particles are widely acknowledged as pervasive contaminants, present in both outdoor and indoor settings, with particularly elevated concentrations in heavily populated metropolitan regions. Indoor exposure may be particularly alarming because restricted ventilation and prolonged duration spent indoors, especially among children and at-risk populations. Upon inhalation, these particles may settle in the upper respiratory tract and subsequently reach the nasal cavity, where they interact with the olfactory epithelium. Subsequently, they may traverse the olfactory nerve, circumventing the protective blood-brain barrier completely. This retrograde transport route facilitates direct access to the olfactory bulb, a cerebral region intimately linked to olfaction and emotional memory. Investigations with aquatic animals, including goldfish, have revealed that extended exposure to polystyrene microplastics disrupts sensory behaviors and induces both functional and structural damage to the olfactory bulb[18]. Gene expression associated with olfactory receptors and brain signalling was considerably modified, suggesting the extensive neurotoxic potential of microplastics even during initial exposure phases.

In mammalian models, maternal exposure during gestation has demonstrated the ability of microplastics to elicit neurological effects across generations. A study using mice revealed that females exposed to water contaminated with polystyrene nanoparticles before mating had offspring with notable neurological impairments[19]. These encompassed modifications in cerebral volume, morphology, and cortical connection. The hippocampus, visual cortex, primary motor and sensory regions, and corpus callosum were significantly impacted. The findings indicate that microplastics can traverse the placental barrier, impacting fatal brain development and potentially resulting in enduring cognitive and behavioral impairments. Another significant channel entails the direct traversal of the blood-brain barrier. Normally, this barrier works as a selective shield, protecting the brain from hazardous substances. Recent research utilizing mouse models have demonstrated that nano plastics, particularly particles smaller than two micrometres, can breach the barrier after ingestion[20]. This capability is affected by the presence of cholesterol molecules, which are intrinsic constituents of cell membranes and can augment the fluidity of the barrier, hence enabling the ingress of foreign particles such as microplastics. Upon entry, these particles may aggregate in different areas of the brain, instigating oxidative stress, neuroinflammation, and mitochondrial dysfunction, which are all precursors to neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis[21]. Recent research has begun to investigate oral exposure as a significant pathway of concern[22]. Microplastics are increasingly present in ubiquitous food items, such as seafood, drinking water, table salt, tea, sugar, and even fresh fruit. Particles consumed via food may gradually traverse the intestinal epithelium into the bloodstream and circulate throughout the body, ultimately arriving at the brain. The prolonged buildup of these particles can insidiously compromise brain function prior to the manifestation of any clinical signs. The penetration of micro and nano plastics into the central nervous system is now a confirmed phenomenon, carrying significant public health consequences. The various entrance routes, such as inhalation, ingestion, transplacental exposure, and penetration of the blood-brain barrier, illustrate the profound integration of these particles within our environment and biological systems. The aggregate impact of these exposures may lead to increasing incidences of cognitive disorders, highlighting the critical necessity for enhanced regulatory oversight, public education, and focused research on mitigation techniques.

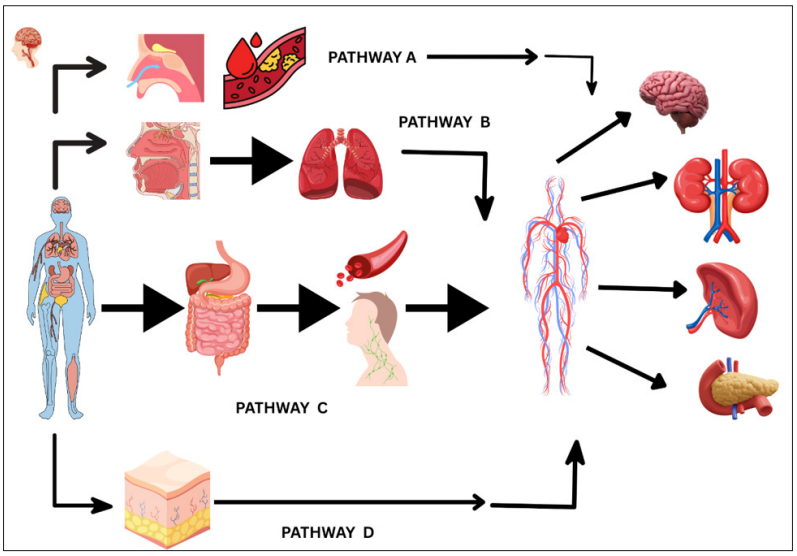

Figure 2: Pathways of microplastic entry and internal distribution in the human body [23-26]. Each pathway is explained in detail below

A. PATHWAY A: Microplastics (Mps) and Nano plastics (Nps) Infiltrate the Brain through Two Primary Pathways: the Olfactory Route and the Blood–Brain Barrier (BBB) Route

The olfactory pathway commences with the intake of airborne microparticles or nanoparticles, which penetrate the nasal cavity and directly interact with the olfactory epithelium. Particles can traverse the olfactory nerve by retrograde axonal transport, ultimately arriving at the olfactory bulb, a structure at the anterior region of the brain responsible for olfactory processing. This pathway allows polymers to circumvent the blood-brain barrier completely. Research indicates that such exposure might result in measurable particle buildup in sensory tissues and notable behavioral changes, including diminished responses to food and social odors, especially in animal models such as goldfish and rodents. The blood–brain barrier (BBB) is a crucial channel, especially for nano plastics measuring less than 2 micrometres. Upon ingestion or inhalation, these particles permeate the bloodstream and disseminate throughout the body. Their capacity to traverse the blood-brain barrier is augmented by the presence of cholesterol molecules, which are essential constituents of the barrier. These chemicals enhance the fluidity of the endothelial cell membranes constituting the blood-brain barrier (BBB), facilitating the penetration of nanoparticles into the central nervous system (CNS). Upon entering the brain, MPs and NPs induce neuroinflammation, oxidative stress, and disrupt neuronal signaling and gene expression, hence presenting a substantial threat to cognitive and neurological health.

B. PATHWAY B: Inhalation Pathway of Microplastic Entry

Inhalation constitutes a principal and direct pathway for the entry of microplastics and nano plastics into the human body. Airborne particles are ubiquitous in both indoor and outdoor settings, particularly in urban and industrial regions where plastic degradation and friction from synthetic fibres facilitate the release of microplastics into the atmosphere. Upon inhalation, these particles initially enter the nose channel and proceed down the respiratory system into the lungs. Ultrafine microplastics and nano plastics can infiltrate lung tissue and reach the circulation via the alveolar capillary barrier, particularly in the alveolar regions where gas exchange transpires. From this point, they are disseminated throughout the body, arriving to remote organs such as the brain, liver, and kidneys. Alongside this systemic circulation route, a more direct brain pathway is present. Certain inhaled particles interact with the olfactory epithelium situated in the superior nasal cavity. These particles may subsequently traverse the olfactory nerve via a mechanism known as retrograde

axonal transport, circumventing the blood-brain barrier entirely. This technique enables microplastics to directly access the olfactory bulb, a vital area of the brain responsible for olfactory processing. Microplastics in the olfactory bulb have been associated with neurological problems, including modified behavioral responses and possible long-term harm to neural tissue. The dual mechanism of bloodstream absorption from the lungs and direct translocation through the olfactory nerve illustrates how inhalation offers a swift and alarming avenue for microplastic entry into systemic circulation and the central nervous system.

C. PATHWAY C: Ingestion Pathway of Microplastic Entry

Ingestion is a prevalent pathway for microplastics to enter the human body. These particles are commonly present in contaminated food and beverages, including shellfish, salt, honey, fruits, vegetables, bottled water, and even tea or beer. Upon ingestion, microplastics traverse the gastrointestinal tract, where some particles may engage with the intestinal lining. A smaller particle size increases the probability of absorption via the intestinal barrier. Microplastics in the small intestine may be absorbed by specialized cells, including M cells in Peyer's patches or enterocytes, via endocytosis. Subsequently, they may be assimilated into the intestinal lymphatic system or straight into the bloodstream through capillaries situated in the intestinal villi. Upon entering systemic circulation, these particles are disseminated throughout the body, possibly accessing critical organs like the liver, kidneys, spleen, and brain. Microplastics in the gastrointestinal system can disturb the gut flora, induce local inflammation, and enhance intestinal permeability, often known as leaky gut. This impaired barrier function may facilitate the ingress of microplastics and other deleterious chemicals into the bloodstream. The ingesting route enables systemic exposure while also presenting considerable dangers to gastrointestinal health and the body's internal environment.

D. PATHWAY D: Dermal Contact Pathway

Dermal contact is regarded as a negligible pathway for microplastic penetration into the body in comparison to inhalation and ingestion. This transpires when the skin encounters surfaces tainted with microplastics or nano plastics, including plastic-laden dust, cosmetic formulations, or contaminated water. The outer layer of healthy skin serves as an effective barrier against most particles; nevertheless, nanoparticles can penetrate more readily due to their minuscule size. The danger of dermal absorption escalates when the skin is compromised, as in the case of cuts, abrasions, or disorders such as eczema that undermine the skin barrier's integrity. In such instances, microplastics, particularly nano plastics, may penetrate through compromised skin and access deeper tissues. Nonetheless, research indicates that the absorption of microplastics in compromised skin is still restricted in comparison to alternative pathways. Nevertheless, continuous or extended skin exposure may result in localized irritation or inflammation, and the potential for systemic absorption cannot be entirely dismissed, particularly for nanoparticles.

2.1 Internal Transport and Distribution

Once microplastics and nano plastics have entered the body through inhalation, ingestion, or dermal contact, they can be absorbed into the bloodstream or the lymphatic system. From these entry points, the particles circulate throughout the body via the cardiovascular system. The bloodstream acts as a transport highway, delivering microplastics to various organs and tissues. These particles can accumulate in organs such as the liver, kidneys, spleen, lungs, and importantly, the brain. Their presence in vital organs is a cause for concern because microplastics have been associated with cellular stress, inflammation, and oxidative damage. The ability of certain nanoparticles to cross protective barriers like the blood brain barrier further raises alarms about potential neurological impacts.

Continuous circulation and accumulation may exacerbate tissue damage and contribute to chronic health conditions, highlighting the significance of understanding internal transport mechanisms for assessing the risks posed by microplastics.

generation of free radicals. Experiments exposing larval zebrafish to microplastics demonstrated increased malondialdehyde levels, an indicator of oxidative stress, and a reduction in antioxidant enzymes such as catalase and glutathione[31-32].

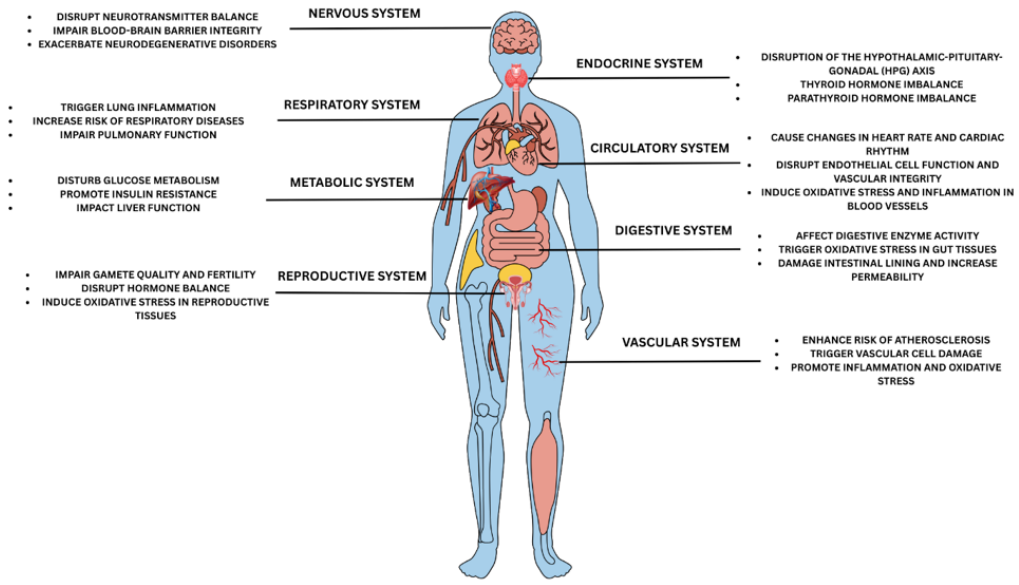

Figure 3: Key bodily systems impacted by micro and nanoplastic exposure along with associated diseases and symptoms[27-28]

3. Molecular Mechanisms Driving the Worsening of Neurodegenerative Diseases Induced by Microplastics: Neurodegenerative Cascade Induced by the Intraneural Migration of Micro and Nano plastics

Microplastics exacerbate neurodegenerative illnesses mainly by inducing oxidative stress in the body[29]. As these particles amass, their deleterious effects intensify, instigating chemical reactions that produce free radicals on their surfaces. Furthermore, the surfaces of microplastics can interact with ambient oxygen, generating secondary reactive species including superoxide and alkyl radicals[30]. These free radicals induce inflammation by impairing essential cellular constituents, including membranes, lipids, proteins, DNA, and lipoproteins. Microplastics infiltrate cells through diffusion, passive transport, or endocytosis, subsequently accumulating in organelles like lysosomes and mitochondria. This buildup disturbs membrane potentials and subsequently induces oxidative stress through the

This imbalance enables free radicals to remain in the body for an extended duration, intensifying cellular damage. The inflammatory response elicited by oxidative stress from microplastics is especially detrimental to the central nervous system because of its elevated lipid content. Activated glial cells secrete pro-inflammatory signalling chemicals that undermine the integrity of the blood-brain barrier, enhancing its permeability [33-34]. This disturbance permits immune cells, including T-cells and macrophages, to infiltrate the central nervous system, inciting acute inflammation and increasing susceptibility to infections. Prolonged exposure to inflammatory stimuli leads to persistent neuroinflammation, creating a detrimental loop of neuronal degeneration. This primarily transpires due to the excessive stimulation of glial cells and the involvement of several cellular signalling pathways, sustaining neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis. Astrocytes, a kind of glial cells crucial for sustaining brain homeostasis, are

significantly engaged in these inflammatory processes [35-37]. Their activity is governed by various signalling pathways, including mitogen-activated protein kinases, calcineurin, the JAK/STAT3 axis, and the nuclear factor kappa B pathway. The JAK/STAT3 pathway serves as a major mediator of astrocyte activation. Upon activation, astrocytes secrete inflammatory mediators, including interleukin-17. This cytokine prompts adjacent glial cells and neurons to generate supplementary pro-inflammatory molecules, including as interleukin-6, tumor necrosis factor alpha, and matrix metalloproteinases. This cascade enlists additional astrocytes to the injured area, establishing a feed-forward loop that perpetuates persistent inflammation. If this mechanism remains unregulated, it results in heightened brain damage and exacerbation of neurodegenerative symptoms. Increased interleukin-17 levels have been regularly noted in illnesses such as multiple sclerosis, Alzheimer's disease, and Parkinson's disease[38]. Furthermore, astrocyte failure exacerbates chronic inflammation through the production of excessive anti-inflammatory cytokines, which paradoxically increases the metabolic demands on these cells. This metabolic load hinders their capacity to regulate essential activities including glutamate uptake, leading to glutamate buildup. Excess glutamate compromises neuronal membrane integrity, facilitates the leakage of cytosolic lactate dehydrogenase, and elevates the generation of reactive oxygen species[39]. These effects additionally disrupt brain metabolism and are associated with cognitive deterioration. Postmortem examinations of Alzheimer's patients have identified aggregates of hyperactive astrocytes adjacent to amyloid-beta plaques, highlighting their contribution to persistent neuroinflammation and the acceleration of disease progression[40-41]. Microglia, a distinct category of glial cells tasked with preserving brain homeostasis and eliminating infected or damaged cells, also significantly contribute to neuroinflammation[42]. Microglia secrete cytotoxins and generate type 1 interferons, crucial to the brain's innate immune response. Nonetheless, when hyperactivated, microglia secrete excessive cytotoxins that harm adjacent healthy tissue, expediting neurodegeneration in conditions such as Alzheimer's and Parkinson's[43]. In Alzheimer's disease, microglia react to misfolded amyloid-beta plaques by secreting cytokines and chemokines. Chronic inflammation induces microglial aggregation around these plaques, facilitating disease development via many pathways[44]. Hyperactive microglia expedite the aberrant phosphorylation of Tau proteins by impairing neuronal synaptic compartments, so exposing additional Tau sites to pathogenic alteration[45]. Moreover, microglia promote the dissemination of aberrant Tau proteins throughout the brain through synaptic pathways, exacerbating synaptic dysfunction and neuronal demise. Therapeutic strategies targeting the modulation of microglial activation are being investigated to potentially impede or decelerate disease development. Inflammation substantially affects the course of Parkinson's disease. This condition is defined by the degeneration of dopaminergic neurons in the substantia nigra and the development of Lewy bodies, which are atypical clusters of alpha-synuclein protein[46]. Hyperactive astrocytes generate surplus alpha-synuclein, facilitating the formation of Lewy bodies. These aggregates stimulate microglia, leading to persistent inflammation and neuronal injury. The inflammation is induced by heightened synthesis of many inflammatory mediators, including tumor necrosis factor alpha, different interleukins, basic fibroblast growth factor, and transforming growth factor beta[47]. The olfactory bulb is among the initial brain regions impacted by Parkinson's disease, with the majority of patients exhibiting olfactory impairments prior to the onset of motor symptoms[48]. Increased concentrations of tyrosine hydroxylase, an enzyme that enhances dopamine production in the olfactory bulb, have been associated with motor deficits. The olfactory bulb volume is markedly diminished in persons with Parkinson's disease relative to healthy individuals[49]. The olfactory

bulb may serve as a potential conduit for microplastics into the central nervous system, hence playing a significant role in the onset or exacerbation of Parkinson's disease pathology[50]. A common clinical characteristic of both Alzheimer's and Parkinson's illnesses is protein fibrillation, wherein misfolded proteins aggregate into amyloid fibrils. Protein fibrillation transpires in three stages: nucleation (lag phase), elongation, and saturation[51]. Research indicates that nanoparticles and microplastics may expedite fibrillation by shortening the nucleation phase and enhancing the rate of fibril production[52]. This mechanism is probably pertinent to the aggregation of amyloid-beta, prion proteins, alpha-synuclein, and Tau proteins noted in neurodegenerative disorders. Multiple sclerosis, a chronic inflammatory disorder characterized by increasing demyelination, gliosis, and axonal injury, is further aggravated by neuroinflammation[53]. In multiple sclerosis, the immune system assaults the myelin sheath of neurons, resulting in plaque development predominantly in the brain's white matter, optic nerves, and spinal cord. These lesions originate from B-cell aggregates that secrete cytokines such as interleukin-6 and granulocyte-macrophage colony-stimulating factor, which subsequently facilitate the development of inflammatory T-cell subtypes and suppress regulatory T-cells[54]. This immunological activation stimulates microglial and astrocyte responses, exacerbating demyelination. Astrocytes uniquely contribute by creating glial scars that obstruct neuronal healing mechanisms. Elements that exacerbate microglial and astrocyte dysregulation, such as microplastic exposure, may hasten the advancement of multiple sclerosis. Chronic inflammation induced by extensive microplastic exposure is becoming a crucial element in the initiation and advancement of neurodegenerative illnesses, including Parkinson's disease, Alzheimer's disease, and multiple sclerosis[55]. The chronic inflammatory milieu fostered by oxidative stress, excessive glial cell activation, and protein aggregation establishes a detrimental cycle that harms neurons and impairs normal brain function. Mitigating microplastic infiltration and its molecular ramifications may be essential in formulating preventive and treatment approaches for these severe illnesses. Table 1 mentions about the key biomarkers associated with micro and nanoplastics (MNP) induced neurotoxicity.

Table 1: Key Biomarkers Associated with Micro and Nanoplastics (MNP)-Induced Neurotoxicity

Category	Biomarkers	Description	References
Oxidative Stress Markers	MDA (Malondialdehyde), 8-OHdG	Indicators of lipid peroxidation and DNA oxidative damage	[56]
Inflammatory Cytokines	TNF-α, IL-6	Key pro-inflammatory markers elevated during neuroinflammation	[57]
Neurodegeneration Indicators	Tau, α-Synuclein	Markers of neuronal damage and neurodegenerative disorders like Alzheimer's or Parkinson's	[58]
Antioxidant Defense Markers	SOD (Superoxide Dismutase), GPx, CAT	Enzymes involved in neutralizing reactive oxygen species	[59]
Apoptosis Markers	Caspase-3, Bax/Bcl-2 ratio	Indicators of programmed cell death in neurons	[60]
Neurotransmitter Alterations	Dopamine, Acetylcholine, GABA levels	Imbalance in neurotransmitter levels linked to cognitive and behavioral changes	[61]
Neurotrophic Factors	BDNF (Brain-Derived Neurotrophic Factor)	Supports survival of existing neurons and growth of new neurons	[62]
Glial Activation Markers	GFAP, Iba-1	Indicate astrocyte and microglial activation hallmarks of neuroinflammation	[63]

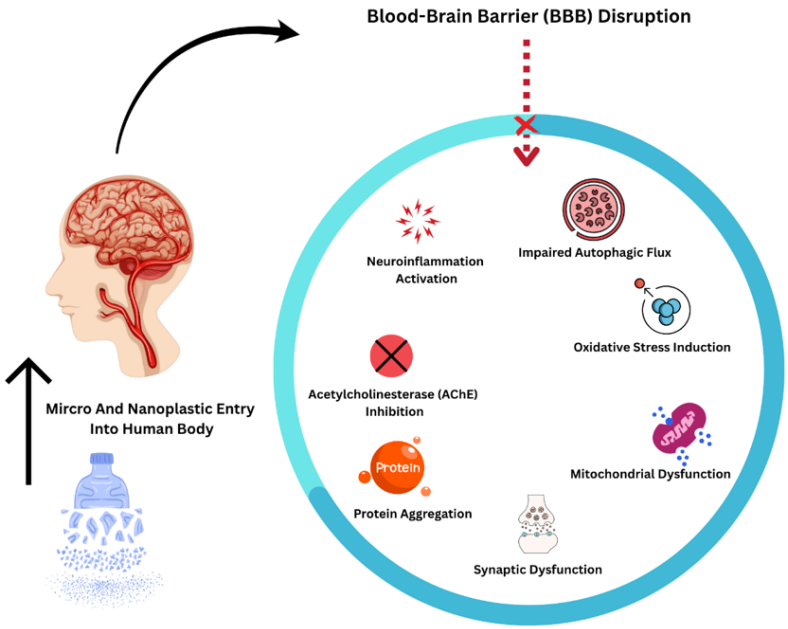

Figure 4: Mechanisms of Microplastic-Induced Neurodegeneration Highlighting Blood-Brain Barrier Disruption, Autophagy Inhibition, and Acetylcholinesterase (AChE) Inhibition [64-65]

4. Impact of Micro and Nano Plastics on the Gut–Brain Axis and its Role in Neurodegeneration

Comprising a complex network of communication channels, the gut-brain axis (GBA) not only preserves gastrointestinal balance but also affects cognitive ability, motivation, and emotions. By combining digestive tasks with neural processes, this complex system helps the gut and the brain to interact constantly. It links many intestinal activities including immune responses, gut barrier control, reflex actions of the enteric nervous system, and hormone signaling within the gastrointestinal tract with the emotional and cognitive areas of the brain[66]. Coordinated interaction of neurological, immunological, and endocrine signals controls the GBA's communication. The gut brain axis is a two-way communication system comprising the enteric nervous system, the central nervous system including the brain and spinal cord, the autonomic nervous system, and the hypothalamic pituitary adrenal axis[67]. Comprising the sympathetic and parasympathetic branches, the autonomic system brings signals from the gut to the brain and from the brain back to the gut. These signals pass via vagal, spinal, and enteric circuits. The response of the body to stress is mostly dependent on the hypothalamic pituitary adrenal axis[68]. It belongs to the limbic system of the brain, mostly in charge of memory and emotional reactions. Environmental stress and raised body levels of inflammatory molecules set this system off. The hypothalamus releases corticotropin releasing factor once triggered, which sets off the pituitary gland to produce adrenocorticotropic hormone. After that, this hormone sets off the adrenal glands to generate cortisol, a main stress hormone influencing many organs including the brain. By means of both nerve based and hormone based communication, the brain can affect vital gut cells including immune cells, epithelial cells, neurons in the gut, smooth muscle cells, Cajal cells, and enterochromaffin cells[69]. The gut flora also affects these same cells; it is now known as a major factor in the gut brain connection. Every human digestive tract contains enteric bacteria. Although every person has a different microbial profile, in healthy individuals the general distribution and relative abundance of main bacterial groups along the intestine usually follow consistency. At least three fourths of the total microbiome are made up of the most dominant bacterial groups, Firmicutes and Bacteroides phyla[70]. Supporting the host's

metabolism and physiological activities, this microbial population is essential for preserving equilibrium and stability in the body all through life.

Recent studies have increasingly acknowledged the gut–brain axis as a pivotal mediator in the onset and advancement of neurodegenerative disorders[71-72]. The gut–brain axis denotes the intricate bidirectional communication network connecting the central nervous system (CNS) with the enteric nervous system (ENS), encompassing neuronal, immunological, and endocrine signalling pathways. This axis preserves homeostasis by modulating immunological responses, metabolic functions, and neurotransmitter synthesis. The disruption of this axis is associated with the etiology of various neurodegenerative illnesses, such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis. Micro and nano plastics (MNPs), pervasive environmental pollutants, have demonstrated the capacity to accumulate in the gastrointestinal system after intake. Their presence can significantly disrupt the fragile equilibrium of the gut microbiota, which is crucial for preserving gut integrity and regulating systemic and brain inflammation[73]. Microbial nanoparticles can produce dysbiosis by selectively enhancing the proliferation of harmful bacterial species while inhibiting good commensals[74]. This microbial dysbiosis can undermine the intestinal barrier, elevating its permeability a condition commonly known as "leaky gut." Heightened intestinal permeability facilitates the transport of bacterial endotoxins, including lipopolysaccharides (LPS), pro-inflammatory cytokines, and MNP particles into systemic circulation[75]. This systemic inflammation functions as a persistent stressor, capable of traversing the blood-brain barrier or activating peripheral immune cells that interact with the central nervous system, resulting in microglial activation and neuroinflammation. Neuroinflammatory processes are pivotal to neuronal dysfunction, synapse loss, and, ultimately, neurodegeneration. Moreover, MNP-induced changes in gut microbiota may hinder the synthesis of neuroactive metabolites, including short-chain fatty acids (SCFAs), which are recognized for their role in regulating microglial function and neuroimmune responses. A deficiency or imbalance of these metabolites may intensify CNS inflammation and increase neuronal susceptibility. Experimental models have started to elucidate the complex effects of MNP exposure on the gut-brain axis[76-78]. Rodent studies demonstrate that prolonged use of nano plastics results in alterations in gut microbial diversity, increased pro-inflammatory markers in both gut and brain tissues, and cognitive and motor function abnormalities [79-80]. These data indicate that MNP-induced gut dysbiosis and inflammation may precede and contribute to central nervous system disease. Considering the pivotal function of the gut–brain axis in neurological well-being, comprehending how MNPs disrupt this axis is essential for clarifying the indirect mechanisms by which environmental plastic pollution heightens the risk of neurodegenerative diseases. Future study should concentrate on elucidating the molecular mechanisms responsible for MNP-induced modifications in gut microbiota, disruption of the intestinal barrier, and systemic immune activation, as well as their effects on neural function. This may enhance our comprehension of MNP neurotoxicity and may also reveal new treatment targets for restoring gut microbiome equilibrium and safeguarding brain health against environmental toxins. Fig. 5 shows Impact of nanoplastic exposure on the gut-brain axis exploring the critical roles of the hypothalamic-pituitary-adrenal (HPA) axis, enteric nervous system (ENS), and microbial-derived short-chain fatty acids (SCFAs) in mediating neuroimmune interactions and gut-brain communication

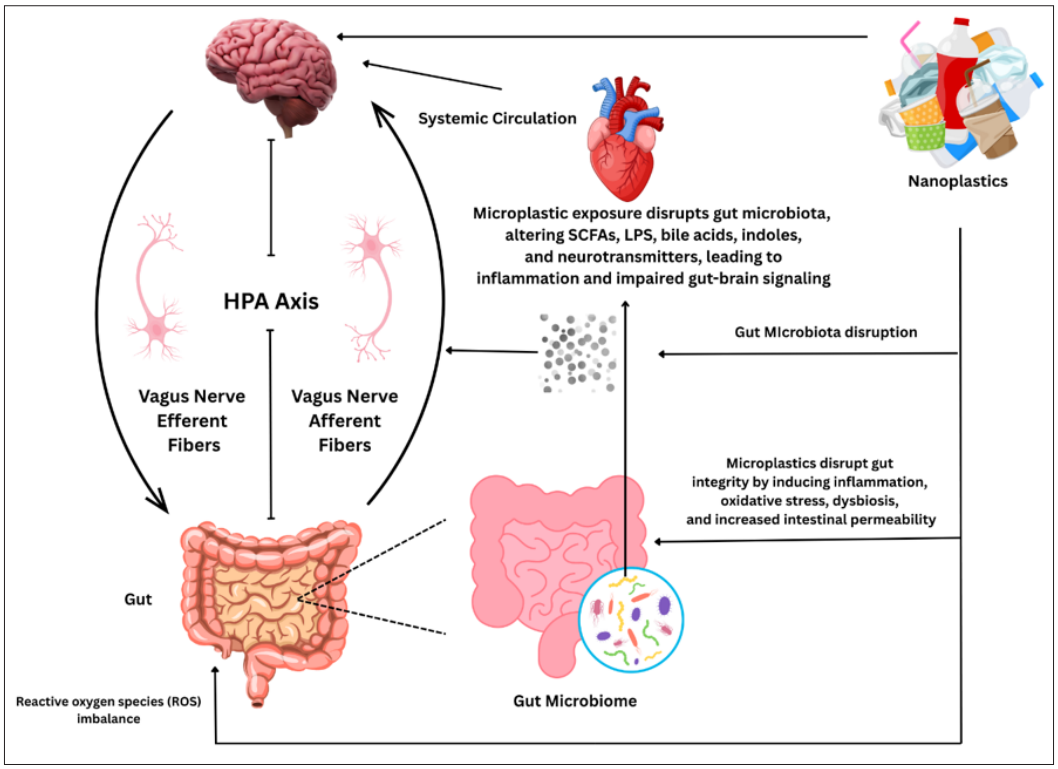

Figure 5: Impact of nanoplastic exposure on the gut-brain axis: exploring the critical roles of the hypothalamic-pituitary-adrenal (HPA) Axis, Enteric Nervous System (ENS), and microbial-derived short-chain fatty acids (Scfas) in mediating neuroimmune interactions and gut-brain communication [81-82]

5. Conclusion and Future Directions

There is a significant connection between environmental pollution and brain health, which is highlighted by the rising body of research that suggests micro and nano plastics are neurotoxic agents. Plastic particles of this size are capable of quietly penetrating biological systems and crossing the blood-brain barrier. This can result in the activation of complicated processes such as oxidative stress and neuroinflammation, both of which are detrimental to neural tissues. Concerns regarding the total neurotoxic burden imposed by widespread plastic contamination are further heightened by the fact that the processes responsible for these nanoparticles are similar to those of other nanoparticles. The neurotoxic effects of micro and nano plastics are largely attributed to the function that oxidative stress plays in the process. Damage to DNA, improper folding of proteins, activation of pathways leading to cell death, and disruption of neurotransmitter activities are some of the impacts that can lead to these consequences. The production of myelin and synaptic plasticity may be impaired as a result of such disruptions, which can hasten the onset of neurodegenerative disorders and contribute to the deterioration of cognitive abilities. There is a possibility that vulnerable populations, such as youngsters who are still developing and adults who are elderly, are particularly at danger from prolonged exposure to these particles. Although these insights have been gained, there are still considerable gaps in our understanding. The amount of direct evidence that brain cells are able to take in particles is minimal, and there is a need for clarification on the precise relationships that exist between exposure dose, particle properties, and neurotoxic results. In order to facilitate risk assessments, it is necessary to do systematic research on the numerous impacts that are brought about by the various types of polymers and additives. The development of more sophisticated imaging tools that can monitor particle mobility and uptake in neural tissues should be the primary focus of study in the future. In addition, it is of the utmost importance to research preventative

therapies, such as antioxidants, which have the potential to attenuate the negative effects that exposure to plastic has on the brain. We will have a better knowledge of the toxicity of these particles if we conduct research that investigates how the form, size, and chemical makeup of the particles influence their capacity to pass through biological barriers. The development of complete models of neurotoxicity caused by micro and nano plastics will require the integration of scientific disciplines such as toxicology, neuroscience, and material science. From the point of view of public health, the prevention of plastic pollution and the reduction of human exposure are of the utmost importance. In conjunction with environmental regulations that are aimed at lowering the amount of waste plastic produced, there is a need for enhanced knowledge of the neurological hazards that are posed by micro and nano plastics. Priority should be given to the development of more secure alternatives to plastic as well as therapy options that are beneficial for people who have been exposed. In conclusion, the danger that micro and nano plastics pose to the health of the brain is an urgent challenge that crosses the gap between environmental science and neuroscience. In order to effectively address this matter, it will be necessary to engage in a coordinated approach that incorporates rigorous scientific research, educated public health policy, and environmentally sustainable behaviors. The protection of brain health in the setting of increasing plastic pollution is absolutely necessary in order to forestall the occurrence of a silent epidemic of neurodegenerative and neurodevelopmental problems in future generations from occurring.

6. Informed Consent Statement

This review article does not involve any new studies with human participants or animals performed by the author. Therefore, informed consent was not applicable.

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8. Figures And Diagrams

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10. Conflict of Interest: None

11. References

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